

## **REMARKS**

Upon entry of these amendments, claims 37, 52, 69, 71-77, 90, and 95 will be pending in the application. Although Applicant does not agree with the Examiner on the present rejections, claims 36, 41, 42, 50-51, 70, 74-75, 78-89, 91-94, and 96 have been cancelled to expedite prosecution of the present case. Applicant reserves the right to prosecute the cancelled subject matter in a continuing application or applications.

### Rejections under 35 U.S.C. § 112, second paragraph

Claims 36, 37, 41, 42, 50-52, and 69-96 are rejected as indefinite for reciting the terms “synthetic gastrin derivative” and “recombinant modified EGF.” Claims 36, 41, 42, 50-51, 70, 78-89, 91-94, and 96 are now cancelled. Applicant will address this rejection as applied to the pending claims.

Applicant notes that the terms “synthetic gastrin derivative” and “recombinant modified EGF” do not appear in claim 69, from which depend claims 71-73, 76-77, and 90, and request withdrawal of the rejection as applied to these claims.

Claims 37, 52, 71, and 95 have been amended to refer to a specific gastrin molecule and a specific EGF molecule. Claims 37, 52, 71, and 95, for example, are now directed to a gastrin 17 molecule having a methionine substituted for leucine at amino acid position 15 and a recombinant human EGF1-53 molecule having a deletion of two C-terminus amino acids at amino acid positions 52 and 53 (see, for example, at page 9, lines 4 to 7 and page 10, lines 8 to 12 of the specification). Because the sequences for gastrin 17 and EGF1-53 are well known in the art (see, for example, Exhibit A (Rehfeld, *Physiological Reviews*, 78: 1087, 1998) and

Exhibit B (U.S. Patent No. 5,158,935)), one skilled in the art would immediately understand which molecules would fall within the scope of the claimed invention.

The Examiner further states that recitation of a specific residue number (e.g., position 15 or 51) in claims 37, 52, 71, or 96 is indefinite as one skilled in the art would not know which amino acid position is referred to. Claim 96 is cancelled. As amended, claims 37, 52, and 71 now refer to specific amino acid positions in a gastrin receptor ligand or an EGF receptor ligand *relative* to the amino acid sequence of the corresponding *wild type* ligand. Based on this amendment, one skilled in the art would immediately recognize which amino acid position is referred to, and this rejection may therefore be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 36, 41, 42, 51, 69, 70, 78-89, 91-95 are rejected as being obvious in view of Nardi et al., (U.S. Patent No. 5,885,956). Claims 36, 41, 42, 51, 70, 78-89 and 91-94 have been cancelled. The rejection is addressed as applied to pending claims 69 and 95.

Claim 69 has been amended to include the subject matter of claims 74 and 75, which are not subject to the rejection. Therefore, claim 69 and its dependent claims 71-73, 76-77, and 90 are non-obvious over Nardi.

Claim 95 has been amended so that it is directed to a method of treating diabetes by administering a gastrin 17 molecule having a methionine substituted for leucine at amino acid position 15 and a recombinant human EGF1-53 molecule having a deletion of two C-terminus amino acids at amino acid positions 52 and 53. Nardi fails to describe or suggest the use of any gastrin ligand or EGF ligand having a mutation, much less those required by claim 95.

Accordingly, Applicants request withdrawal of the rejection for obviousness.

Obviousness-Type Double Patenting

Claims 36, 42, 51, 69, 70, 72, 73, 85-89, and 91-95 are rejected for obvious-type double patenting doctrine in view of claims 19-20, 22, 24-25, and 32-33 of copending U.S. Serial No. 10/843,780 (hereinafter the '780 application). In applying this rejection, the Examiner states that claims 19-20, 22, 24-25, and 32-33 of the '780 application are directed to methods and compositions for treating diabetes using a gastrin/CCK receptor ligand and an EGF receptor ligand in an amount sufficient to induce the differentiation of pancreatic islet precursor cells to mature insulin-secreting cells. The Examiner therefore concludes that the '780 application, in teaching that the efficacy of treatment may be measured by monitoring blood glucose levels, is not patentably distinct from the present claimed invention.

Claims 36, 42, 51, 70, 85-89, and 91-94 are now cancelled. The rejection is traversed to the extent it is applied to the claims as amended.

Claim 69 submitted herewith, from which depends claims 72 and 73, is directed to a method of treating diabetes using a gastrin/CCK receptor ligand and an EGF receptor ligand, such that the first effective dose of the gastrin/CCK receptor ligand in the composition is between about 2-fold and about 100-fold greater by weight than the second effective dose of the EGF receptor ligand or the first effective dose is at least about equivalent by weight to the second effective dose (support found in original claims 74 and 75, now cancelled). Therefore, Applicants submit that amended claims 69, 72, and 73 are patentably distinct from claims 19-20, 22, 24-25, and 32-33 of the '780 application.

Amended claim 95 is directed to a method for treating diabetes involving the administration of gastrin 17 having a methionine substituted for leucine at position 15, and a

**Applicant: Brand**  
**U.S.S.N. 10/044,048**

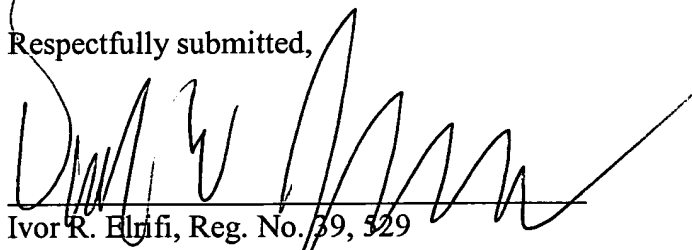
recombinant human EGF1-53 having a deletion of two C-terminus amino acids at positions 52 and 53 and having a neutral amino acid substituted at position 51. Thus, it is submitted that amended claim 95 is patentably distinct from claims 19-20, 22, 24-25, and 32-33 of the '780 application.

In view of the foregoing amendments and arguments, Applicant respectfully requests that the obviousness-type double patenting rejection be withdrawn.

Applicant respectfully submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

A petition for extension of time is enclosed. Although no additional fees are believed to be due, the Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 24492-006.

Respectfully submitted,



Ivor R. Elrifi, Reg. No. 39, 329

David E. Johnson, Reg. No. 41,874

Attorneys for Applicants

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY  
AND POPEO, P.C.

Tel: (617) 542-6000

Customer No. 30623

Dated: August 5, 2005

TRA 2061410v1